REMARKS

Reconsideration of this application is respectfully requested.

Claims 68-74 were previously pending in this application. These claims have been canceled in favor of new claims 75-90. Accordingly, newly added claims 75-90 are presented for further examination.

New Claims

Claims 75-89 are directed to a packaging cell line. Claim 75 is independent and it recites "[a] packaging cell line for propagating a viral vector independent of a helper virus, said viral vector comprising a nucleic acid component and at least two different non-nucleic components, wherein one of said non-nucleic acid components has a tropism for said cell line and the other non-nucleic acid component has a tropism for a target cell which is different from said cell line." Claim 75 goes on to recite that "said nucleic acid component and said non-nucleic acid components [are] capable of forming a specific complex or complexes, wherein said sequence or sequences for the viral vector nucleic acid component is stably integrated in the genome of said cell line, and said sequence or sequences for the non-nucleic acid components of said viral vector are introduced into said packaging cell line by transient expression, episomal expression or stably integrated expression." In terms of elemental distinctions from former and now canceled independent claim 68, claim 75 refers to a viral vector "comprising a nucleic acid component and at least two different non-nucleic components." In so reciting, the new claims are now directed to the multitropic aspects of Applicants' invention. Claim 75 also refers to "a tropism for said cell line" and "a tropism for a target cell which is different from said cell line," again, two recitations directed to multitropic

aspects of Applicants' claimed packaging cell line. Support for claim 75 and the multitropic features of the present invention are found variously in the specification. See, for example, page 30, last paragraph, through page 36.

Claim 76 depends from claim 75 and it recites "wherein said viral vector comprises a retrovirus or retroviral sequences." Support for claim 76 is found in the specification, page 15, second full paragraph; page 23, second full paragraph; and page 28, fourth and fifth lines from the bottom of the page. The language of this claim mimics that of originally filed claims 7, 24, 30 and 54. In claim 77, also depending from claim 75, the viral vector is defined as comprising nucleic acid sequences derived from genomic DNA, cDNA, or fragments of either or both of the foregoing." Support for the foregoing language is drawn from page 37, second full paragraph, in the specification.

Claims 78-80 are directed to the species of the packaging cell line and the target cell. Claim 78 recites that "said packaging cell line and said target cell are from different species." Claim 79 recites that "said packaging cell line is a non-human animal species and said target cell is human." In claim 80, the "non-human animal species is murine." Support for the subject matter of claims 78-80 is drawn from the specification, page 31, first paragraph; page 32, last paragraph, through page 34, first paragraph.

Claim 81 recites that the target cell is selected from "T cells, liver cells, bone marrow cells, epithelial cells, and a combination of any of the foregoing." Support for this language is found on page 26, last full paragraph.

Claims 82-87 cover coding embodiments for the viral vector produced in Applicants' claimed packaging cell line. Claim 82 recites that "the viral vector produced from said packaging cell line codes for a protein of interest that is expressed in said target cell." Support for the foregoing claim language is taken

from the specification, page 14, second and third lines from the bottom of the page. Claim 83 defines the viral vector produced from the packaging cell line as coding "for an antisense RNA that is transcribed in said target cell." Support for this language is also found in the specification, page 19, last sentence of the full paragraph. In claim 84, the viral vector produced from the packaging cell line is defined as coding "for a protein of interest that is expressed in said target cell and for an antisense RNA that is transcribed in said target cell." The subject matter of claim 84 is drawn from the specification, page 14, second and third lines from the bottom of the page; and page 19, last sentence of the full paragraph. Claim 85 depends from claim 84 and it defines the antisense RNA as being "complementary to an mRNA coding for a undesirable protein in said target cell." Support for claim 85 is found in the specification, page 19, last sentence of the full paragraph. Claim 86 is multiply dependent and it defines that antisense RNA as being "part of a chimeric RNA molecule that comprises sequences from small nuclear RNAs (snRNAs)." The language in claim 86 can be found on page 19, full paragraph, in the specification. Claim 87 defines the snRNAs of claim 85 as being any of "U1, U2, U3, U4, U5, U6, U7, U8, U9, U10 or U11." These members are listed in the specification, page 15, last three lines.

Claims 88-90 were drafted in light of the rejection under 35 U.S.C. §112, second paragraph, involving the term "native." Thus, claim 88 recites "wherein said nucleic acid component comprises sequences derived from a virus that is native to said cell line." Claim 89 recites "wherein said nucleic acid component comprises sequences derived from a virus that is native to said target cell." Claim 90 combines the recitations of claims 87 and 88 by reciting "wherein said nucleic acid component comprises sequences derived from a virus that is native to said cell line and sequences derived from a different virus that is native to said target cell."

The recitation of the term "native" in new claims 87-90 is believed to be clear and definite such that its meaning would be understood by the skilled artisans. Moreover, the present recitation in the claims conforms to usage in the art, the specification at hand, and the subject matter being claimed herein.

It is believed that the subject matter of the new claims is fully supported by Applicants' originally filed disclosure. Entry of new claims 75-90 is respectfully requested.

The Rejection Under 35 U.S.C. §102(b)

Claims 68-74 stand rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Salmons et al. ["Targeting of Retroviral Vectors for Gene Therapy," Human Gene Therapy 4:129-141 (1993)] or Smith et al. ["Viral Vectors in Gene Therapy," Ann. Rev. Microbiol. 49:807-818 (1995)]. In the Office Action (pages 2-3), the Examiner stated:

> This rejection is maintained for reasons of record in the previous Office Action (Paper #7) and for reasons outlined below.
>
> Applicants have amended claim 68 to insert the word "localized" prior to "complex". Applicants assert that neither Salmons et al. nor Smith et al. teach the claimed localized specific complex.
>
> Applicant's arguments filed 11/30/00 have been fully considered but they are not persuasive. The recited limitation of a specific "localized" complex does not distinguish the claims over Salmons et al. or Smith et al. As previously noted by the examiner, the Salmons et al. and Smith et al. references both recite packaging cell lines which comprise a viral (retroviral) vector comprising a nucleic acid component and a non-nucleic acid component (i.e. gag, pol or env proteins) being capable of forming a specific complex with each other in the context of a viral vector particle. The aforementioned complexes must be "localized" to the extent that they are localized to parts of the cell where the viral particles are formed by the specific complexing of vector nucleic acids and proteins such as gag or pol, etc. The complexes are also localized in that the non-nucleic acid

components are specifically localized and complexed with the nucleic acid component of the vector in the context of formation of the viral vector particle.

The anticipation rejection is respectfully traversed.

As indicated in the opening remarks above, new claims 75-90 have been added above. As set forth in independent claim 75 from which each of claims 76-90 ultimately depend, a packaging cell line is claimed for propagating a viral vector independent of a helper virus. This claim recites that the viral vector comprises a nucleic acid component and at least two different non-nucleic components, "*wherein one of said non-nucleic acid components has a tropism for said cell line and the other non-nucleic acid component has a tropism for a target cell.*" Unlike the present invention, neither of the cited Salmons or Smith papers disclose or suggest the use or inclusion of a viral vector in a packaging cell line in which the viral vector has two different non-nucleic acid components, one having a tropism for the cell line and the other having a tropism for a target cell.

In view of the lack of identity of materials elements between the present invention and the cited documents, Applicants respectfully request reconsideration and withdrawal of the anticipation rejection.

The Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 69 and 71-73 stand rejected for indefiniteness under 35 U.S.C. §112, second paragraph. In the Office Action (page 3) the Examiner stated:

> Claim 69 is vague in the recitation of the phrase "...cell line is native to said viral vector." It is unclear if by "native" to the viral vector applicants are indicating that the cell line is naturally capable of being infected by the virus or is capable of being infected by the virus and is capable of supporting replication of the virus, etc.

> Claims 71-73 are vague for reasons of record in the previous Office Action and for reasons outlined below.
>
> Applicants have traversed this rejection by asserting that the skilled artisan would appreciate the metes and bounds of the claimed invention.
>
> In response, the examiner notes that the claim language is unclear. If for example, a promoter of the recited vector is from a retrovirus genome and a termination sequence is from an AAV genome, is a coding sequence from the same AAV genome a non-native sequence to the vector or is it native to the vector because it is also from the AAV genome which is part of the vector?

The indefiniteness rejection is respectfully traversed.

With respect to the recitation of "native" in former and now canceled claim 69, it is believed that the presentation of new claims 88-90 obviates the basis for this rejection. The use of the terms "native" or "non-native" in former and canceled claims 71-73 is also believed to be obviated by these newly added claims.

As indicated above, claim 88 recites "wherein said nucleic acid component comprises sequences derived from a virus that is native to said cell line." In turn, claim 89 recites "wherein said nucleic acid component comprises sequences derived from a virus that is native to said target cell." Claim 90 recites "wherein said nucleic acid component comprises sequences derived from a virus that is native to said cell line and sequences derived from a different virus that is native to said target cell." It is respectfully submitted that a person skilled in the art would appreciate the meaning and the metes and bounds of the subject matter embraced by claims 88-90 and the use of the term "native" as recited in these claims.

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the indefiniteness rejection.

Submission of Information Disclosure Statement

As soon as an indication has been received that the present application has been returned to Group 1600, Applicants' attorney intends to submit an Information Disclosure Statement (IDS) in order to bring a number of documents to the attention of the Examiner and The Patent Office.

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SUMMARY AND CONCLUSIONS

Claims 75-90 have been added in place of claims 68-74, the latter claims having been canceled.

The claim fee for adding claims 75-90 is $149 based upon the fee for one additional claim above the 20 claims previously paid for (1 X $9 = $9) and the first time presentation of multiple dependent claims ($140). The Patent and Trademark Office is hereby authorized to charge the requisite $149 claim fee to Deposit Account No. 05-1135. No other fee or fees are believed to be due in connection with this Amendment or the accompanying filings. If any other fee or fees are due, however, for either this response or the accompanying filings, The Patent and Trademark is authorized to charge the amount of any such fee(s) to Deposit Account No. 05-1135, and to credit any overpayment thereto.

Applicants respectfully submit that all of the instant claims are in allowable condition. Should it be deemed helpful or necessary, the Examiner is respectfully invited to telephone the undersigned at (212) 583-0100 to discuss the subject application.

Respectfully submitted,

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